



A YEAR AFTER DOCTORS BEGAN IMPLANTING THE ABIOCOR IN DYING PATIENTS,
THE PROSPECTS OF THE DEVICE ARE UNCERTAIN

The Trials of an **Artificial** **HEART**

By Steve Ditlea

The permanent replacement of a failing human heart with an implanted mechanical device has long been one of medicine's most elusive goals. Last year this quest entered a crucial new phase as doctors at several U.S. hospitals began the initial clinical trials of a grapefruit-size plastic-and-titanium machine called the AbioCor. Developed by Abiomed, a company based in Danvers, Mass., the AbioCor is the first replacement heart to be completely enclosed within a patient's body. Earlier devices such as the Jarvik-7, which gained worldwide notoriety in the 1980s, awkwardly tethered patients to an air compressor. In contrast, the AbioCor does not require tubes or wires piercing the skin. In July 2001 Robert L. Tools, a 59-year-old former Marine whose heart had become too weak to pump effectively, became the first recipient of this artificial heart.

Over the next nine months, surgeons replaced the failing hearts of six more patients with the AbioCor. But the initial trials have had mixed results. As of press time, five of the seven patients had died: two within a day of the implantation procedure, one within two months, and two within five months. (Tools died last November.) One of the two survivors has lived for more than eight months with the device, the other for more than six months. Because all the patients were seriously ill to begin with—only people deemed likely to die within a month were eligible for implantation—Abiomed officials argue that the artificial heart is proving its worth. The company has acknowledged, however, that a flaw in the device's attachments to the body might have led to the formation of the blood clots that caused strokes in three of the patients.

ABIOCOR, an artificial heart made of plastic and titanium, has been in clinical trials for the past year.

With the clinical trials only a year old, it is obviously too early to say whether the AbioCor will be a breakthrough or a disappointment. If the U.S. Food and Drug Administration decides that the device shows promise, it may allow Abiomed to implant its artificial heart in patients who are not as severely ill as those in the initial group. Company officials hope that eventually the rate of survival after implantation will surpass the rate after heart transplants (about 75 percent of the recipients of donor hearts are still alive five years after the transplant). Fewer than 2,500 donor hearts become available every year in the U.S., whereas more than 4,000 Americans are on waiting lists for transplants; for many of those patients, AbioCor could be a lifesaver.

But the artificial heart is competing against less radical treatments, one of which has already proved quite successful. Doctors have been able to restore adequate cardiac function in thousands of patients by attaching a pump to the left ventricle, the chamber most likely to fail. These ventricular-assist devices were originally intended as a short-term therapy for people awaiting transplants, but recent studies show that the pumps can keep patients alive for two years or more [see box on pages 66 and 67]. Meanwhile other studies have overturned generations of medical wisdom by suggesting that the human heart can repair itself by generating new muscle tissue. Researchers are now racing to develop therapies using stem cells that could help the heart heal [see box on page 68].

Heart History

THE ORIGINS of the artificial heart go back half a century. In 1957 Willem J. Kolff (inventor of the dialysis machine) and Tetsuzo Akutsu of the Cleveland Clinic replaced the heart of a dog with a polyvinyl chloride device driven by an air pump. The animal survived for 90 minutes. Seven years later President Lyndon B. Johnson established an artificial-heart program at the National Institutes of Health. In 1969 Denton A. Cooley of the

LIKE A HUMAN HEART, the AbioCor has chambers for pumping blood on its left and right sides. Oxygenated blood from the lungs flows into and out of the left chamber, and oxygen-depleted blood from the body flows into and out of the right chamber. Between the chambers is the mechanical equivalent of the heart's walls: a hermetically sealed mechanism that generates the pumping motions.

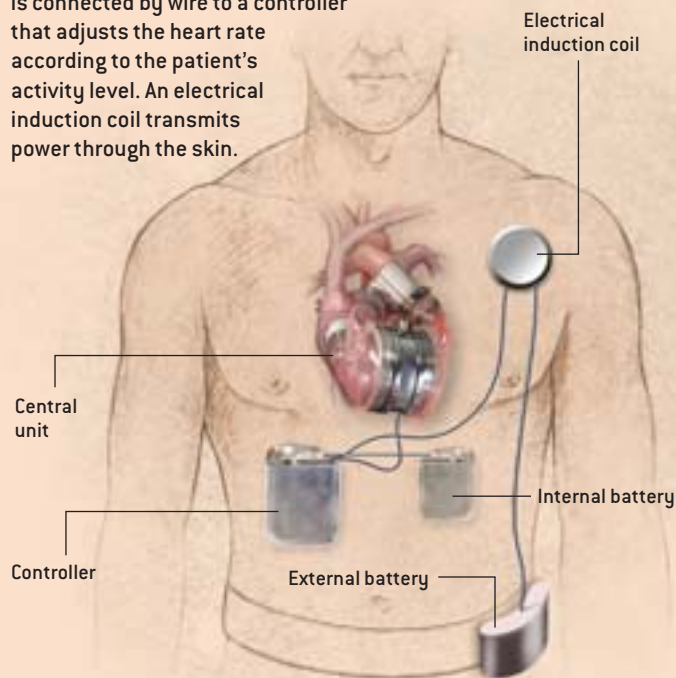
At the center of this mechanism, an electric motor turns a miniaturized centrifugal pump at 5,000 to 9,000 rotations a minute. The pump propels a viscous hydraulic fluid; a second electric motor turns a gating valve that allows the fluid to alternately fill and empty from the two outer sections of the pumping mechanism. As fluid fills the left section, its plastic membrane bulges outward, pushing blood out of the AbioCor's left chamber. At the same time, hydraulic fluid empties from the right section and its membrane deflates, allowing blood to flow into the device's right chamber.

The AbioCor's four valves are made of plastic and configured like natural heart valves. The inflow conduits are connected to the left and right atria of the excised heart, and the outflow conduits are fitted to the arteries. The device weighs about one kilogram and consumes about 20 watts of power. The internal battery, electrical induction coil and controller module add another kilogram to the implanted system. Lithium-ion batteries worn on the patient's belt continuously recharge the internal battery using the induction coil. A bedside console can also be used as a power source and monitoring system. —S.D.

Overview/AbioCor Heart

- The goal of implanting a permanent mechanical substitute for a failing human heart was all but abandoned after controversial attempts in the 1980s. The clinical trials of the AbioCor, a new artificial heart designed to be completely enclosed in a patient's body, began in July 2001.
- The trials have had mixed results so far. Of the seven severely ill patients who received the AbioCor, two died within a day of the implantation, one within two months, and two within five months. Although the artificial heart did not cause infections, three patients suffered strokes.
- If the survival rate of the AbioCor improves, it could eventually become an alternative for people on the long waiting lists for heart transplants. But the device may have to compete with less radical treatments such as ventricular-assist devices and therapies using stem cells.

THE CENTRAL UNIT of the AbioCor is connected by wire to a controller that adjusts the heart rate according to the patient's activity level. An electrical induction coil transmits power through the skin.



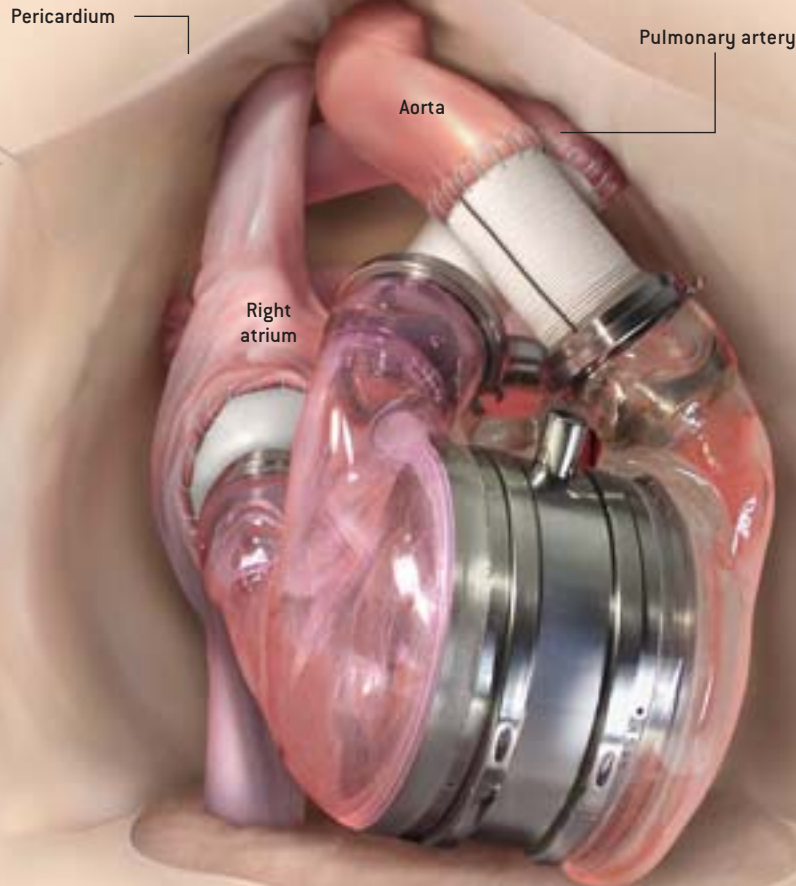
HOW THE ABIOCOR WORKS

THE ABIOCOR is attached to the remnants of the right and left atria of the patient's excised heart. The grafts used in the first six patients had plastic struts designed to keep the atrial walls apart; autopsies showed clotting on these struts.

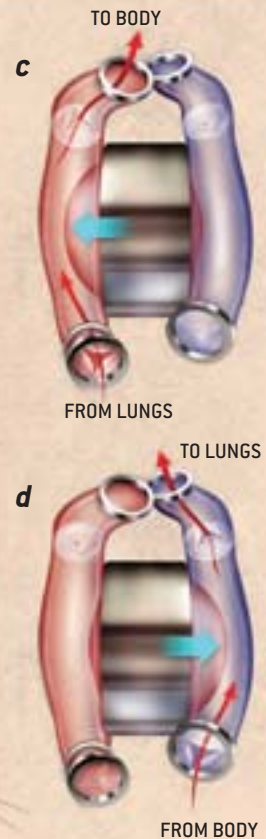
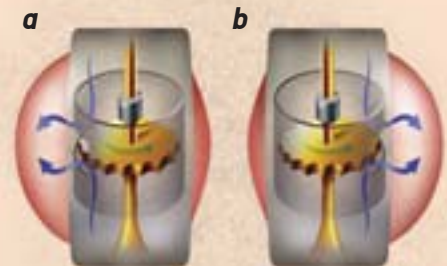
DETAIL OF ATRIAL GRAFT



IN THIS ARTIST'S rendering, the AbioCor is shown after implantation in the patient's body. The pericardium, the membrane surrounding the heart, is peeled back.



THE ABIOCOR'S pumping mechanism mimics the beating of a human heart by propelling hydraulic fluid back and forth. (The diagrams below show the device from the rear perspective.) A centrifugal pump turns continuously in one direction while a gating valve alternately shunts the hydraulic fluid to the left and right (a and b). When the fluid flows to the left, it pushes a plastic membrane into the AbioCor's left chamber, pumping oxygenated blood to the body (c). When the fluid flows to the right, it pushes a membrane into the right chamber, pumping oxygen-depleted blood toward the lungs (d).



ETHICS OF THE HEART

The AbioCor trials revive some troubling questions

DURING THE CLINICAL TRIALS of the Jarvik-7 artificial heart, medical ethicists voiced concern about the suffering of the patients and the intense media coverage that descended on them. Now those issues have surfaced anew with the human testing of the AbioCor. So far ethicists give mixed grades to Abiomed (the maker of the device), the doctors and the press.

"The core ethical issues for the patient remain the same," says Arthur Caplan, director of the Center for Bioethics at the University of Pennsylvania School of Medicine. "First, can you get truly informed consent from a desperate, dying person? Dying is extremely coercive. There's very little you can't get a dying person to consent to." In Abiomed's favor, he rates the firm's 13-page consent form as "very strong" in terms of disclosing risks, and he commends the company's funding of independent patient advocates to inform patients and their families. But

Caplan wonders whether the right patients are enrolled in the trials: "I've argued that for some treatments it doesn't make sense to test first in the most severely ill, because you have an impossible time sorting out what's caused by the illness and what's caused by the device."

George J. Annas, a professor at the Boston University School of Public Health, contends that the consent procedure for the AbioCor "should be much more detailed about how you're going to die. No one's going to live for a long time on one of these. You have to plan for death. How is it going to happen? Who's going to make the decision and under what circumstances?" In two cases during the clinical trials, family members agreed to shut off the AbioCor's power, overriding its alarms, so a terminally failing patient could die.

Another source of controversy has been Abiomed's policy of limiting the release of information from the trials. For example, company officials will not announce a patient's identity until 30 days after an implantation (leaks at the hospital, however, have sometimes forced

them to do so sooner). Although the policy has prevented a repeat of the media frenzy surrounding the Jarvik-7 trials, some ethicists have emphasized the need for full disclosure of the medical problems encountered during the human testing. Renee Fox, a social sciences professor at the University of Pennsylvania, notes that Abiomed's reporting of negative developments has been timely, for the most part. But, she adds, "there has been a tendency by the company and the physicians to interpret adverse events as not due to the implanted heart. In each case there has been an attempt to say that this is due to the underlying disease state of the patient rather than any harm that the device may have done."

Ethicists point out that journalists have erred, too, by writing overoptimistic stories about the AbioCor. It was a hopeful cover story in *Newsweek* that convinced Robert L. Tools to volunteer for the first implant. Says Ronald Munson, a professor of philosophy of science and medicine at the University of Missouri at St. Louis, "The press shouldn't evangelize a medical procedure." —S.D.

Texas Heart Institute in Houston implanted an artificial heart into a person for the first time, but only as an emergency measure. The device was intended as a bridge to transplant—it kept the patient alive for 64 hours until a human heart could be found for him. (The patient received the transplant but died two and a half days later.) The next artificial-heart implant was not attempted until 1981. The patient lived for 55 hours with the bridge-to-transplant device before receiving a human heart.

Then came the most publicized clinical trials in modern medicine: cardiac surgeon William DeVries's four permanent implants of the Jarvik-7 artificial heart. When DeVries performed the first cardiac replacement in 1982 at the University of Utah Medical Center, patient Barney B. Clark became an instant celebrity. His medical status was reported almost daily. Reporters tried to sneak into the intensive care unit in laundry baskets or disguised as physicians. By the time Clark died 112 days later—from multiple organ failure after suffering numerous infections—the media had provided a detailed chronicle of the medical problems and discomfort he had experienced.

Nearly two years later DeVries performed his next Jarvik-7 implant, this time at Norton Audubon Hospital in Louisville, Ky., on patient William Schroeder. Schroeder survived on the artificial heart for 620 days, the longest of anyone to date, but

it took a tremendous toll on him: strokes, infections, fever and a year of being fed through a tube. The third Jarvik-7 recipient lived for 488 days, and the fourth died after just 10 days. Although several hospitals successfully used a slightly smaller version of the Jarvik-7 as a bridge-to-transplant device for hundreds of patients, most medical professionals abandoned the idea of a permanent artificial heart.

But an engineer named David Lederman believed that the concept still held promise. Lederman had worked on developing an artificial heart at the medical research subsidiary of Avco, an aerospace company, and in 1981 he founded Abiomed. He and his colleagues closely followed the clinical trials of the Jarvik-7 and considered ways to improve it. The external air compressor that powered the device was bulky and noisy. Infectious bacteria could easily lodge where the tubing pierced the patient's skin. And inside the heart itself were surface discontinuities where platelets and white blood cells could coagulate into a thrombus, a solid clot that could circulate in the blood and lodge in the brain, causing a stroke.

In 1988 the National Heart, Lung and Blood Institute at the NIH decided to cut off support for replacement-heart research and instead channel funds to ventricular-assist pumps. Lederman went to Washington along with representatives from oth-

er research teams to lobby against the change. They convinced a group of senators from their home states to help restore NIH support, resuscitating research programs at two universities (Utah and Pennsylvania State) and two companies (Nimbus in Rancho Cordova, Calif., and Abiomed). Today Abiomed is the last artificial-heart developer left from that group. The company has received nearly \$20 million in federal research grants. Its government funding ended in 2000, but that same year Abiomed raised \$96 million in a stock offering.

Lederman and his colleagues are doggedly pursuing a medical technology whose time others believe may have already come and gone. In the conference room at Abiomed's headquarters in an office park north of Boston, Lederman attributes his firm's tenacity to its team of researchers: "No one else had the commitment to say there is no alternative to success. This is important stuff. I take pride in the fact that we took it so seriously." It is also evident that for Lederman this is a personal matter: in 1980 his father died suddenly of a heart attack.

Designing AbioCor

THE ABIOCOR is not powered by an air compressor as the Jarvik-7 was. Hidden behind the device's central band of metal is the heart of this heart: a pair of electric motors driving a pump-and-valve system. This pumping mechanism propels hydraulic fluid back and forth, causing a pair of plastic membranes to beat like the inner walls of a human heart [see box on pages 62 and 63].

But this innovation was only the start. To be truly self-contained, the device needed a small, implantable controller that could vary the heart rate to match the patient's activity level. The controller developed by Abiomed is the size of a small paperback; implanted in the patient's abdomen, it is connected to the artificial heart by wire. Sensors inside the heart measure the pressure of the blood filling the right chamber—the blood returning to the heart from the body—and the controller adjusts the heart rate accordingly. The rate can range from 80 to 150 beats a minute. If the clinical trials show that this control system is adequate, it could be shrunk down to a single microchip that would fit on the AbioCor's central unit.

Abiomed also developed a way to power the artificial heart's motors without the use of skin-penetrating wires, which can leave the patient prone to infections. An internal battery implanted in the patient's abdomen can hold enough charge to sustain the heart for 20 minutes. This battery is continuously recharged through electromagnetic induction—the same process used in electric toothbrushes. The internal battery is wired to a passive electrical transfer coil under the patient's skin. Another coil outside the patient's skin, wired to an external battery, transmits power through the skin tissue with minimal radiation and heat. The patient can wear the external battery on a belt, along with a separate monitor that alerts the patient if the battery's charge runs low.

A major concern was to design the AbioCor so that it could pump blood without creating clots. When Lederman had worked for Avco, he had conducted four years of research on the interaction between blood and synthetic materials, studying



ABIOCOR RECIPIENTS: Robert L. Tools (*above*), shown holding an artificial heart like the one in his chest, became the first AbioCor patient in July 2001. He died in November after suffering a severe stroke. The second recipient, Tom Christerson (*below*), has lived the longest with the AbioCor—more than eight months as of press time. Shown here with a physical therapist at Jewish Hospital in Louisville, Ky., Christerson returned home in April.



the reaction rates of various coagulation processes. Essentially the AbioCor minimizes clotting by making sure that the blood cells do not have time to stick together. Blood flows swiftly through the device, and there are no areas where pooling can occur. All the surfaces of the device that are in contact with blood are made of Angioflex, a biologically inert polyurethane plastic. The contact surfaces are also extremely smooth because clots can form on irregular surfaces. Says Lederman, "We had to make a system that was totally seamless."

Trial and Error

AFTER TESTING its artificial heart in calves and pigs, Abiomed received permission from the FDA in January 2001 to begin clinical trials in humans. The FDA would determine the success of the trials by reviewing the patients' survival rates and quality of life, as measured by standard assessment tests. Only patients who were ineligible for a heart transplant could volunteer for the implantation. The size of the AbioCor also ruled out certain patients: the device can fit inside the chests of only half of adult men and 18 percent of adult women. (Abiomed is developing a smaller, second-generation heart that would fit most men and women.) For each procedure, Abiomed agreed to pay for the device and its support. Hospitals and doctors participating in the trials would donate facilities and care. The total cost of each implantation and subsequent treatment: more than \$1 million.

On July 2, 2001, the first AbioCor was implanted in Robert L. Tools at Jewish Hospital in Louisville, Ky., by surgeons Laman A. Gray, Jr., and Robert D. Dowling in a seven-hour operation. Tools had been suffering from diabetes and kidney failure as well as congestive heart failure. Before the heart replacement, he could barely raise his head. After the procedure, Tools experienced internal bleeding and lung problems, but within two months his kidney function had returned to normal and he had enough strength to be taken on occasional outings from the hospital. His doctors hoped he would be able to go home by Christmas. Tools's bleeding problems persisted, however, making it difficult for doctors to administer the anticoagulant drugs intended to prevent clot formation. On November 11 he suffered a severe stroke that paralyzed the right side of his body. He died 19 days later from complications following gastrointestinal bleeding.

The second recipient of the AbioCor, a 71-year-old retired businessman named Tom Christerson, has fared much better so far. Surgeons at Jewish Hospital implanted the device in Christerson on September 13, 2001. After a steady recovery, he left the hospital in March to take up residence in a nearby hotel, where he and his family could learn how to tend to the artificial heart on their own. The next month he returned to his home in Central City, Ky. In the following weeks, Christerson continued his physical therapy and visited Jewish Hospital for weekly checkups. His car was wired so that he could use it as a power source for his artificial heart.

At the Texas Heart Institute, O. H. "Bud" Frazier—the surgeon who has the record for performing the most heart transplants—implanted the AbioCor into two patients. One lived with the device for more than four months before dying of com-



HEARTMATE PUMP, the most widely used ventricular-assist device, is implanted in a patient's abdomen, as shown in this artist's rendering. Attached to a failing left ventricle, the device pumps oxygenated blood to the body.

plications from a stroke; the other died within a day of the implantation, succumbing to uncontrolled bleeding after spending 20 hours on the operating table. Implantations have also been performed at the University of California at Los Angeles Medical Center and Hahnemann University Hospital in Philadelphia. The Los Angeles patient lived for a little less than two months before heart support was withdrawn following multiple organ

COURTESY OF THORATEC

HEART HELPERS

Ventricular-assist devices emerge as an alternative to heart replacement

IN NOVEMBER 2001, soon after human testing of the AbioCor began, researchers reported that another clinical trial had demonstrated the benefits of a less drastic treatment for heart failure. The left ventricular assist device [LVAD]—a pump implanted in the chest or abdomen and attached to the heart's left ventricle, the chamber that pumps oxygenated blood to the body—had been developed as a short-term therapy for patients awaiting heart transplants. But the trial showed that LVADs can keep patients alive for two years or more, and the Food and Drug Administration is expected to approve the devices for long-term use.

The study evaluated 68 patients with implants of the HeartMate, the most widely used LVAD, and 61 patients who received medical therapy, including potent cardiac drugs. After a year, more than half of those with LVADs were still alive, compared with only one quarter of those on medical therapy. At two years, the survival rates were 23 percent for the LVAD group and 8 percent for the medical group. The longest stint on the HeartMate is now more than three years; the longest survivor of the medical group died after 798 days. "There are still 21 patients ongoing with the devices," notes Eric Rose, surgeon in chief at Columbia Presbyterian Medical Center in New York City and principal investigator for the trial. "This sets a new benchmark for treating the disease."

The HeartMate, made by Thoratec in Pleasanton, Calif., is far from perfect. Many of the implanted test subjects suffered serious infections because the device is connected to an external battery by a skin-piercing tube. Other HeartMate patients died from mechanical malfunctions such as motor

failure. The Philadelphia patient, 51-year-old James Quinn, received the AbioCor on November 5, 2001. Although he suffered a mild stroke in December, the next month he was discharged from the hospital to a nearby hotel. This past February, however, he was readmitted to the hospital with breathing difficulties. Doctors treated him for pneumonia, which became life-threatening because his lungs were already weakened by chron-



JARVIK 2000 is the only assist device small enough to fit within the left ventricle. Robert K. Jarvik, inventor of the Jarvik-7 artificial heart, now develops assist devices rather than replacement hearts.

failure. But Thoratec has already improved on the current version of the device and is developing second- and third-generation systems designed to last eight and 15 years, respectively.

Another LVAD, called the LionHeart, made by Arrow International in Reading, Pa., is a fully implantable system with no skin-piercing tubes or wires. Now in clinical trials, the LionHeart uses an electrical induction coil like the AbioCor's to transmit power through the skin. The MicroMed DeBakey VAD is also fully implantable, but it propels blood in a steady flow rather than pumping it like a natural heart. Proponents of this technology tout its efficiency and reliability; critics argue that a pulsating heartbeat is needed to keep blood vessels clear. Cardiac pioneer Michael E. DeBakey, who performed the first successful coronary bypass in 1964, developed the device in collaboration with one of his patients, David Saucier, a NASA engineer

who had had heart transplant surgery.

Robert K. Jarvik, inventor of the Jarvik-7 artificial heart and now CEO of New York City-based Jarvik Heart, has introduced the Jarvik 2000, the only assist device small enough to be lodged inside the left ventricle. Like the DeBakey VAD, the Jarvik 2000 pumps blood in a steady flow. The device is currently in trials for bridge-to-transplant use and has been implanted in some patients for long-term use as well. Jarvik believes the device could help a less severely damaged heart to repair itself, perhaps in combination with stem cell treatments [*see box on next page*]. Another potential combination therapy might be the use of LVADs with the steroid clenbuterol to strengthen the heart. In a test reported last year, Magdi Yacoub of Harefield Hospital in London administered clenbuterol to 17 patients with implanted LVADs. In five of the patients, the hearts recovered enough to allow the removal of the LVADs. —S.D.

ic emphysema and pulmonary hypertension. Quinn was placed on a ventilator to help him breathe, but his recovery was slow. By mid-May, though, his condition was improving, and doctors began to wean him from the ventilator.

In January, Abiomed reported preliminary findings from the clinical trials at a press conference. Lederman noted that the artificial heart had continued to function under conditions that

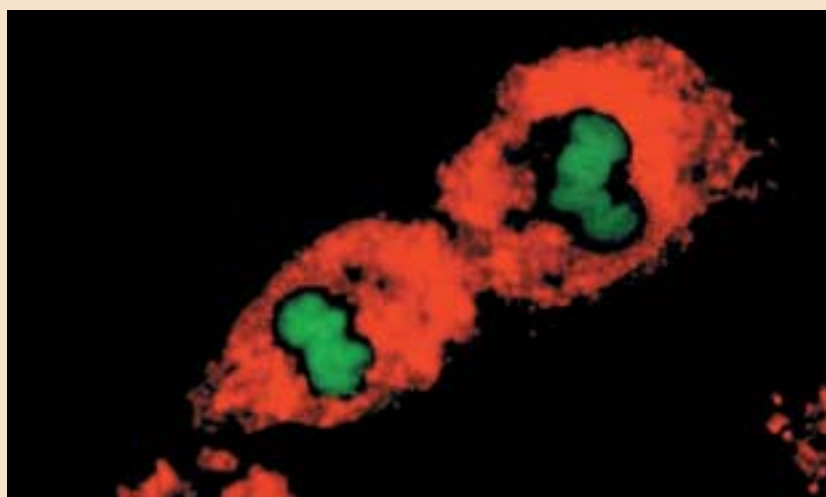
MENDING BROKEN HEARTS

Stem cells may prove to be the best medicine for injured hearts

EVERY SO OFTEN, unexpected findings turn scientific wisdom upside down. Two studies recently published in the *New England Journal of Medicine* have refuted the long-held notion that the human heart cannot repair itself after a heart attack or other injury. The research indicates that new muscle cells can indeed grow in adult hearts and that they may arise from stem cells, the undifferentiated building blocks of the body. The discovery may pave the way for therapies that encourage natural healing.

Research teams at the New York Medical College (NYMC) in Valhalla, N.Y., and the University of Udine in Italy conducted the iconoclastic experiments. The first study found chemical markers indicating new growth of muscle cells in heart samples taken from patients who had died four to 12 days after a myocardial infarction (the medical term for a heart attack). The second study, which involved the postmortem examination of female hearts transplanted into men, showed the presence of stem cells with Y chromosomes in the donated hearts. Although these stem cells could have migrated from the male recipient's bone marrow, they could have also come from the cardiac remnant to which the female heart was attached.

"Our paper suggests the possibility that cardiac stem cells may exist," says Piero Anversa, director of the Cardiovascular Research Institute at the NYMC. "We need to determine all the characteristics that prove that we are



HEART MUSCLE CELL, or myocyte, is shown dividing in this microscope image of tissue taken from a patient who died shortly after a heart attack. The evidence suggests that, contrary to prevailing medical opinion, new myocytes can grow to replace damaged ones.

dealing with a primitive cell in the heart. And then we need to see whether we can mobilize these cells in areas of heart damage to promote repair."

Other medical researchers are pursuing regenerative cardiac therapies with stem cells taken from other parts of the body. Philippe Menasché, professor of cardiovascular surgery at the Bichat-Claude Bernard Hospital in Paris, has injected primitive muscle cells from patients' legs into damaged areas of their hearts during cardiac bypass surgery. Initial results from the clinical trials have been encouraging, showing thickening of heart muscle walls with functional tissue. But Menasché is cautious about therapeutic outcomes. "At best, these cells may help enhance other treatments," he says. "Imagining that you'll be able to completely regenerate an

infarcted heart is probably unrealistic."

But some biotechnology firms are entertaining even wilder hopes. Advanced Cell Technology, the Worcester, Mass.-based company that gained notoriety last year with its human cloning experiments, has already turned stem cells into beating heart cells and is trying to create transplantable patches for repairing larger areas of damage. "Eventually we want to engineer a full heart," says Robert Lanza, the company's vice president for medical and scientific development. The task would require generating cardiac muscle and blood vessel tissue as well as fabricating a dissolvable biological scaffolding material for building the heart. How far off is a biological artificial heart? According to Lanza, "We could produce a functioning heart in 10 years, with clinical trials in maybe 15 years." —S.D.

could have damaged or destroyed a natural heart, such as a severe lack of oxygen in the blood and a fever of 107 degrees Fahrenheit. Also, no patient had suffered an infection related to the device. But Abiomed acknowledged a design flaw in the artificial heart's connections to the body. The AbioCor is attached to remnants of the atria of the patient's excised heart; autopsies on two patients had shown clotting on the plastic struts of thimble-size "cages" that were intended to maintain the separation of the remaining atrial walls [see illustration on page 63]. Because these clots could cause strokes, Abiomed declared that

it would no longer use the plastic cages when implanting the AbioCor. The cages were needed to test the device in calves but are unnecessary in humans.

In early April, Abiomed announced that it would not be able to meet its original schedule of implanting the AbioCor in 15 volunteers by the end of June. The company said that it wanted to devote further study to its first six cases. But a week later doctors at Louisville's Jewish Hospital performed another implantation, the first using an AbioCor without the plastic cages. The artificial heart functioned properly, but the 61-year-

old patient died within hours of the procedure after a clot lodged in his lungs. According to Laman Gray, who performed the operation with colleague Robert Dowling, the clot did not originate in the AbioCor.

The surgeons who have worked with the AbioCor remain convinced of the device's potential, despite the recent setbacks. Frazier of the Texas Heart Institute believes the formation of clots in the AbioCor's plastic cages was a complication that could not have been anticipated. "Fortunately, this one can be corrected," he says. "It's not something inherently wrong in the device." Gray concurs: "In my opinion, it's very well designed and is not thrombogenic at all. The problem has been on the in-flow cage. I'm truly amazed at how well it has done in initial clinical trials." (Both surgeons consulted on the AbioCor's design and were responsible for much of its testing in animals.)

But not everyone is as sanguine as Frazier and Gray. "Total heart replacement by mechanical devices raises a number of questions that have not been addressed in this small group of patients," says Claude Lenfant, director of the National Heart, Lung and Blood Institute. "What quality of life can a total-heart-replacement patient expect? Will there be meaningful clinical benefits to the patient? Is the cost of this therapy acceptable to society?" And Robert K. Jarvik, the developer of the Jarvik-7 device that made headlines 20 years ago, now argues that permanent artificial hearts are too risky. "Cutting out the heart is practically never a good idea," he says. "It was not known in 1982 that a heart can improve a lot if you support it in certain very common disease states. That's why you should cut out the heart only in the most extreme situations."

Heart of the Matter

AS THE ABIOCOR TRIALS continue, the most crucial objective will be reducing the incidence of strokes. Doctors had originally hoped to guard against this risk by prescribing low levels of anticoagulant drugs, but some of the test subjects were so severely ill that they could not tolerate even these dosages. Because these patients had medical conditions that made them susceptible to internal bleeding, determining the best dosage of anticoagulants became a delicate balancing act: giving too much might cause the patient to bleed to death, and giving too little might cause a stroke.

Despite the need for more refinement, Lederman is satisfied with the clinical results to date. The initial goal of the trials was to show that AbioCor could keep the patients alive for at least 60 days, and four of them surpassed that mark. Says Lederman, "If most of the next patients go the way the first ones have gone but without unacceptable complications such as strokes, we plan



JUST BEFORE IMPLANTING the AbioCor into patient Tom Christerson, surgeons Laman A. Gray, Jr. (left), and Robert D. Dowling (right) evacuate the air from the artificial heart to prevent blood clotting. The procedure was performed on September 13, 2001, at Louisville's Jewish Hospital.

to ask the FDA to authorize clinical use of the system for patients who are on their last breath. We think we have a convincing argument that we can give patients with less than 30 days to live many months of quality life." But some medical ethicists have questioned this approach, saying that people at death's door might consent to any procedure, no matter what the consequences [see box on page 64].

And then there is the issue of how to define an acceptable quality of life. In 1981 Jarvik wrote that for the artificial heart to achieve its goal "it must be forgettable"—that is, the device should be so unobtrusive and reliable that patients would be able to ignore it [see "The Total Artificial Heart," by Robert K. Jarvik; *SCIENTIFIC AMERICAN*, January 1981]. Does the AbioCor meet that standard? Tools's wife, Carol, says that her husband was aware that his old heartbeat had been replaced by the AbioCor's low, steady whir. "Sometimes he'd lie there, and he would listen to it," she says. "But other times he would forget it... [He] always knew it was there, because he still had to power it. It's not like replacing a hip." Still, she believes that the quality of life during his last months was good: "He had a chance to live quite well, although unfortunately, it was shorter than we would have liked." She adds, "He never had any regrets about it."

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MORE TO EXPLORE

More information about Abiomed, the manufacturer of the AbioCor, is available at www.abiomed.com

The Web site of the Implantable Artificial Heart Project at Jewish Hospital in Louisville, Ky., is www.heartpioneers.com

The Texas Heart Institute in Houston: www.tmc.edu/thi

The National Heart, Lung and Blood Institute at the National Institutes of Health: www.nhlbi.nih.gov/index.htm